

chain nodes:
1 2 3 4 5 6 8 11

chain bonds:
1-2 1-6 2-3 2-11 3-4 4-5 5-8 exact/norm bonds : 2-3 2-11 3-4 4-5 5-8 exact bonds : 1-2 1-6

G1:0,S

Match level:
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:Atom 8:CLASS 11:CLASS
Generic attributes:

6:

Saturation

: Unsaturated

=> s l1

SAMPLE SEARCH INITIATED 17:34:08 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED -178 TO ITERATE

100.0% PROCESSED 178 ITERATIONS 2 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE** BATCH **COMPLETE**

PROJECTED ITERATIONS:

2760 TO 4360

PROJECTED ANSWERS:

2 TO

2 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 17:34:23 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 3888 TO ITERATE

100.0% PROCESSED 3888 ITERATIONS

SEARCH TIME: 00.00.01

21 ANSWERS

L3-

21 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

155.84 156.05

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FILE COVERS 1907 - 16 Dec 2004 VOL 141 ISS 25 FILE LAST UPDATED: 15 Dec 2004 (20041215/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13 .

14 L3

=> d 14 1-14 bib abs hitstr

L4

```
2004:739958 CAPLUS
AN
      141:260542
DN
      Preparation of nitric oxide releasing prodrugs of diaryl-2-(5H)-furanones
TI
      as selective cyclooxygenase-2 inhibitors
IN
      Berthelette, Carl; Li, Lianhai; Sturino, Claudio; Wang, Zhaoyin
PΑ
      U.S. Pat. Appl. Publ., 19 pp.
SO
      CODEN: USXXCO
DT
      Patent
      English
LA
FAN.CNT 1
      PATENT NO.
                                KIND
                                         DATE
                                                         APPLICATION NO.
                                                                                      DATE
                                ----
                                         -----
                                                         _______
PΤ
      US 2004176331
                                 Α1
                                         20040909
                                                         US 2004-790288
                                                                                       20040301
      WO 2004103955
                                 Α1
                                         20041202
                                                         WO 2004-CA314
                                                                                       20040301
                AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
           W:
                CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
                GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
                NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
           TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
                BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
                TD, TG
PRAI US 2003-452124P
                                 Ρ
                                         20030305
os
      MARPAT 141:260542
GΙ
```

ANSWER 1 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

$$R^{1}$$
 R^{2}
 R^{3}
 R^{2}
 R^{3}
 R^{3}
 R^{4}
 R^{2}
 R^{3}
 R^{4}
 R^{2}
 R^{3}
 R^{4}
 R^{2}
 R^{3}

II

Ι

AB Title compds. I [X = (CH2)n; n = 3-6; R1 = SO2Me, SO2NH2, SO2NHCOCF3, etc.; R2, R3 = H, halo, alkoxy, etc.; R4 = CO-alkyl, CO(CH2)mNR5R6; m = 1-4; R5, R6 = H, halo-substituted alkyl] and their pharmaceutically

IT

CN

acceptable salts were prepared For example, O-alkylation of AgNO3 by bromide II (Z = Br), e.g., prepared from Rofecoxib in 6-steps, afforded nitrooxyhexyl II (Z = -ONO2). In human blood PGE2 inhibition production assays, nitrooxyhexyl II (Z = -ONO2) exhibited an IC50 value of 0.22 μM . Of note, the "unconverted prodrugs" of compds. I are inactive inhibitors of COX-1 and COX-2 activity. Compds. I are claimed useful for the treatment of cyclooxygenase-2 mediated diseases or conditions. 754242-01-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nitric oxide releasing prodrugs of diarylfuranones as selective COX-2 inhibitors)

RN 754242-01-8 CAPLUS

Benzeneacetic acid, α -[2-(acetyloxy)-1-[4-(methylsulfonyl)phenyl]ethylidene]-, 7-(nitrooxy)heptyl ester, (α Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c} \text{AcO} \\ \text{Z} \\ \text{O} \\ \text{O} \\ \text{O} \end{array} \begin{array}{c} \text{O} \\ \text{(CH2)} \\ \text{7} \\ \text{O} \\ \text{NO} \\ \text{2} \end{array}$$

```
ANSWER 2 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN
     2004:267282 CAPLUS
DN
     140:287165
TI
     Manufacturing process for NO-donating compounds such as NO-donating
     diclofenac
     Andersson, Johan; Belli, Aldo; Cannata, Vincenzo; Hedberg, Martin;
IN
     Palmgren, Andreas; Schuldei, Sigrid; Stroem, Marika; Villa, Marco
PΑ
     Astrazeneca UK Limited, UK; Astrazeneca AB
SO
     PCT Int. Appl., 68 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                          KIND
                                 DATE
                                              APPLICATION NO.
                                                                      DATE
                          ----
PI
     WO 2004026808
                           Α1
                                 20040401
                                              WO 2003-SE1465
                                                                      20030918
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
         BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI SE 2002-2801
                           Α
                                 20020920
     SE 2003-1476
                           Α
                                 20030520
os
     CASREACT 140:287165; MARPAT 140:287165
AB
     NO-Donating compds. MLnAmCO2XONOp [M = residue of an NSAID, COX-1
     inhibitor or COX-2 inhibitor; L = O, S, CO2, (un) substituted CONH, NH, CO,
     CH2, CH2CO, CH2CONH, CH2CO2; A = (un)substituted alkylene; X = carbon
     linker; m, n = 0-3; p= 1, 2] are prepared by treating MLnAmCO2H with HOXOH,
     treating MLnAmCO2XOH with RSO2Cl [ R = alkyl, (un) substituted Ph, CH2Ph,
     halogen, CF3, C4F9], and treating MLnAmCO2XO3SR with nitrate.
     substantially crystalline form of 2-[2-(nitrooxy)ethoxy]ethyl
     {2-[(2,6-dichlorophenyl)amino]phenyl}acetate is reported.
IT
     676125-87-4P
     RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
     (Preparation)
        (manufacturing process for NO-donating compds. such as NO-donating
        diclofenac)
RN
     676125-87-4 CAPLUS
CN
     Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[2-[2-
     (nitrooxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)
```

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
L4
     ANSWER 3 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
     2004:41217
AN
                   CAPLUS
     140:111135
DN
ΤI
     Preparation of nitrosated nonsteroidal antiinflammatory compounds
     Earl, Richard A.; Ezawa, Maiko; Fang, Xinqin; Garvey, David S.; Gaston,
IN
     Ricky D.; Khanapure, Subhash P.; Letts, Gordon L.; Lin, Chia-En;
     Ranatunge, Ramani R.; Richardson, Stewart K.; Schroeder, Joseph D.;
     Stevenson, Cheri A.; Wey, Shiow-Jyi
PΑ
     Nitromed, Inc., USA
     PCT Int. Appl., 145 pp.
SO
     CODEN: PIXXD2
DT
     Patent
     English
T.A
FAN.CNT 1
     PATENT NO.
                            KIND
                                    DATE
                                                 APPLICATION NO.
                                                                           DATE
                                                 _____
                            ____
                                    _ _ _ _ _
PΙ
     WO 2004004648
                             A2
                                    20040115
                                                 WO 2003-US21026
                                                                           20030703
     WO 2004004648
                             А3
                                    20041028
              AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
              PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
              UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
              KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
              FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
              BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2004024057
                                    20040205
                             Α1
                                                US 2003-612014
PRAI US 2002-393111P
                             Р
                                    20020703
     US 2002-397979P
                             Ρ
                                    20020724
     US 2002-418353P
                             Р
                                    20021016
     US 2003-449798P
                             Р
                                    20030226
     US 2003-456182P
                             Ρ
                                    20030321
OS
     MARPAT 140:111135
GI
```

Title compds. RnRmHC-CO-X [Rm = H, alkyl; Rn = 4-((thiophen-2-yl)carbonyl)phenyl, 3-(benzoyl)phenyl, etc.; X = Y-alkyl-aryl, etc.; Y = O, S; I] are prepared For instance, naproxen is coupled to 2,2'-thiodiethanol (CH2Cl2, DMAP, EDCI) and treated with Ac2O/HNO3 at 0° to give II. I are nitrosated nonsteroidal antiinflammatory drugs (NSAIDs) used alone or are combined with one compound that donates, transfers or releases nitric oxide, stimulates endogenous synthesis of nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor or is a substrate for nitric oxide synthase. The invention provides methods for treating inflammation, pain, fever, gastrointestinal disorders, etc.

II

IT 646509-75-3P, 2-[N-[2-(Nitrooxy)ethyl]carbamoyl]oxy]ethyl

```
(2S)-2-(6-methoxy-2-naphthyl)propanoate 646509-99-1P,
     [N-Methyl-N-[[[[2-(nitrooxy)ethyl]oxy]carbonyl]methyl]carbamoyl]methyl
     (2S) -2-(6-methoxy-2-naphthyl)propanoate 646510-05-6P,
     [N-Methyl-N-[[[[3-(nitrooxy)propyl]oxy]carbonyl]methyl]carbamoyl]methyl
     (2S) -2-(6-methoxy-2-naphthyl)propanoate 646510-09-0P,
     [N-Methyl-N-[[N-[2-(nitrooxy)ethyl]carbamoyl]methyl]carbamoyl]methyl
     (2S) -2-(6-methoxy-2-naphthyl)propanoate 646510-17-0P,
     [[[2-[[2-(Nitrooxy)ethyl]sulfonyl]ethyl]oxy]carbonyl]methyl
     (2S)-2-(6-methoxy-2-naphthyl)propanoate 646510-88-5P,
     2-[[(2S)-2-(6-Methoxy-2-naphthyl)propanoyl]oxy]ethyl 3-(nitrooxy)propyl
     ethane-1,2-dioate 646511-50-4P, [[[2-[[2-
     (Nitrooxy)ethyl]sulfonyl]ethyl]oxy]carbonyl]methyl 2-(6-methoxy-2-
     naphthyl)propanoate
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (preparation of naproxen-derived nitrosated antiinflammatory compds.)
RN
     646509-75-3 CAPLUS
CN
     2-Naphthaleneacetic acid, 6-methoxy-α-methyl-, 2-[[[[2-
     (nitrooxy)ethyl]amino]carbonyl]oxy]ethyl ester, (<math>\alpha S) - (9CI)
     INDEX NAME)
```

Absolute stereochemistry.

$$\begin{array}{c} \text{Me} \\ \text{S} \\ \text{O} \\ \text{NO}_2 \\ \end{array}$$

Absolute stereochemistry.

RN 646510-05-6 CAPLUS
CN 2-Naphthaleneacetic acid, 6-methoxy-α-methyl-, 2-[methyl[2-[3-(nitrooxy)propoxy]-2-oxoethyl]amino]-2-oxoethyl ester, (αS)- (9CI) (CA INDEX NAME)

RN 646510-09-0 CAPLUS

CN 2-Naphthaleneacetic acid, 6-methoxy- α -methyl-, 2-[methyl[2-[[2-(nitrooxy)ethyl]amino]-2-oxoethyl]amino]-2-oxoethyl ester, (α S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 646510-17-0 CAPLUS

Absolute stereochemistry.

RN 646510-88-5 CAPLUS

CN Ethanedioic acid, 2-[(2S)-2-(6-methoxy-2-naphthalenyl)-1-oxopropoxy]ethyl 3-(nitrooxy)propyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Me O O O
$$(CH_2)_3$$
 NO NO $(CH_2)_3$ NO $(CH_2)_4$ NO $(C$

RN 646511-50-4 CAPLUS

CN 2-Naphthaleneacetic acid, 6-methoxy-α-methyl-, 2-[2-[[2-(nitrooxy)ethyl]sulfonyl]ethoxy]-2-oxoethyl ester (9CI) (CA INDEX NAME)

Page 9

```
ANSWER 4 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
T<sub>1</sub>4
ΑN
      2004:2684 CAPLUS
DN
      140:73178
ΤI
     Nitroxy derivatives of non-steroidal anti-inflammatory compounds as
      selective inhibitors of cyclooxygenase-2 for the treatment of inflammation
IN
     Del Soldato, Piero; Santus, Giancarlo
PΑ
     Nicox S.A., Fr.
     PCT Int. Appl., 49 pp.
SO
      CODEN: PIXXD2
DT
      Patent
LΑ
     English
FAN.CNT 1
      PATENT NO.
                             KIND
                                      DATE
                                                    APPLICATION NO.
                                                                               DATE
      -----
                             ----
                                      ______
                                                    ------
PΙ
     WO 2004000300
                              A1
                                      20031231
                                                    WO 2003-EP6651
                                                                               20030624
          W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
               CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
               KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
               BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI IT 2002-MI1399
                                     20020625
                              Α
     MARPAT 140:73178
AB
      The present invention relates to compds. able to inhibit selectively the
      enzyme cyclooxygenase-2 (COX-2) without inhibiting substantially the
      enzyme COX-1. Specifically, the present invention concerns nitroxy
      derivs. of non-steroidal anti-inflammatory compds., which are able to
      inhibit selectively the enzyme COX-2. The compds. of the invention are
     useful in the treatment and/or prophylaxis of inflammatory processes.
IT
     302543-75-5 302543-76-6 302543-77-7
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)
         (nitroxy derivs. of non-steroidal anti-inflammatory compds. as
         selective inhibitors of cyclooxygenase-2 for treatment of inflammation)
RN
     302543-75-5 CAPLUS
CN
     D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, (aS)-6-methoxy-
     \alpha-methyl-2-naphthaleneacetate (ester) (9CI) (CA INDEX NAME)
```

Absolute stereochemistry.

RN 302543-76-6 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, α-methyl-4-(2-methylpropyl)benzeneacetate (ester) (9CI) (CA INDEX NAME)

RN 302543-77-7 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy) butyl ester, 2-fluoro- α -methyl[1,1'-biphenyl]-4-acetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

GT

```
ANSWER 5 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN
       2004:2666 CAPLUS
DN
       140:65191
ΤI
       Oral pharmaceutical liquid drugs containing nitrate ester NSAIDs having
       improved bioavailability
IN
       Del Soldato, Piero; Santus, Giancarlo; Macelloni, Cristina
PA
       Nicox S.A., Fr.
SO
       PCT Int. Appl., 46 pp.
       CODEN: PIXXD2
DT
       Patent
LA
       English
FAN.CNT 1
       PATENT NO.
                                     KIND
                                                DATE
                                                                 APPLICATION NO.
                                                                                                    DATE
                                     - - - -
                                                -----
                                                                  -----
PΙ
       WO 2004000273
                                      A1
                                                20031231
                                                                 WO 2003-EP6496
                                                                                                    20030620
             W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
                   GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
                   BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI IT 2002-MI1392
                                      Α
                                               20020625
```

$$\begin{array}{c|c} CH_2-CO-O & - CH_2 \\ & & \\ NH & \\ C1 & & \\ \end{array}$$

The present invention relates to new pharmaceutical compns. for the administration of liquid drugs in solid oral forms, said compns. comprising one or more active ingredients, one or more surface-active agents and optionally a co-surfactant and/or an absorption enhancer absorbed on a solid inert carrier. An emulsion was prepared containing I 100, Cremophor EL 50, Phospholipon 80H 50, Aerosil 200 100, and Explotab 100 g.

IT 639067-65-5 639067-67-7 639067-69-9

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral pharmaceutical liquid drugs containing nitrate ester NSAIDs having improved bioavailability)

RN 639067-65-5 CAPLUS

CN 2-Naphthaleneacetic acid, 6-methoxy- α -methyl-, 10-(nitrooxy)decyl ester, (α S)- (9CI) (CA INDEX NAME)

RN 639067-67-7 CAPLUS

CN L-Cysteine, N-acetyl-, 4-(nitrooxy) butyl ester, α -methyl-4-(2-methylpropyl) benzeneacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 639067-69-9 CAPLUS

CN L-Cysteine, N-acetyl-, 4-(nitrooxy) butyl ester, 2-fluoro- α -methyl[1,1'-biphenyl]-4-acetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
ANSWER 6 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
L4
    2003:818296 CAPLUS
AN
    139:302040
DN
ΤI
    Nitrooxy derivatives of antiinflammatory/analgesic compounds for the
    treatment of arthritis
    Del Soldato, Piero
IN
    Nicox S.A., Fr.
PA
    PCT Int. Appl., 71 pp.
SO
    CODEN: PIXXD2
DТ
    Patent
    English
LA
FAN.CNT 1
    PATENT NO.
                        KIND
                                DATE
                                           APPLICATION NO.
                                                                   DATE
     ----
                                            -----
                                                                   _____
PΙ
    WO 2003084550
                         Α1
                                20031016
                                           WO 2003-EP3183
                                                                   20030327
        W: AE, AG, AL, AU, BA, BB, BR, BZ, CA, CN, CO, CR, CU, DM, DZ, EC,
            GD, GE, HR, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA,
            MG, MK, MN, MX, NO, NZ, OM, PH, PL, SG, TN, TT, UA, US, UZ, VN,
            YU, ZA
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI IT 2002-MI773
                         Α
                                20020411
OS
    MARPAT 139:302040
AΒ
    Antiinflammatory and/or antiinflammatory/analgesic compds. having the
     formula A(B)b0(C)c0-N(O)s [A contains radical of nonsteroidal
    antiinflammatory or nonsteroidal antiinflammatory/analgesic drug; B, C =
    bivalent linking group; s = 1, 2; b0, c0 = 0, 1 (with proviso)], and salts
    thereof, are disclosed for use in the treatment of arthritis.
IT
    302543-75-5 497818-53-8 612478-28-1
    RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment
       of arthritis)
     302543-75-5 CAPLUS
RN
    D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, (αS)-6-methoxy-
    \alpha-methyl-2-naphthaleneacetate (ester) (9CI) (CA INDEX NAME)
```

Absolute stereochemistry.

RN 497818-53-8 CAPLUS CN L-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, (αS) -2-fluoro- α -methyl[1,1'-biphenyl]-4-acetate (ester) (9CI) (CA INDEX NAME)

RN 612478-28-1 CAPLUS

CN L-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, (αS) - α -methyl-4-(2-methylpropyl)benzeneacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L4 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
- AN 2003:499717 CAPLUS
- DN 140:314514
- TI Nitric oxide-donating nonsteroidal anti-inflammatory drugs inhibit the growth of various cultured human cancer cells: Evidence of a tissue type-independent effect. [Erratum to document cited in CA138:378736]
- AU Kashfi, Khosrow; Rayyan, Yaser; Qiao, Leon L.; Williams, Jennie L.; Chen, Jie; Del Soldato, Piero; Traganos, Frank; Rigas, Basil
- CS American Health Foundation, Valhalla, NY, USA
- SO Journal of Pharmacology and Experimental Therapeutics (2003), 306(1), 421 CODEN: JPETAB; ISSN: 0022-3565
- PB American Society for Pharmacology and Experimental Therapeutics
- DT Journal
- LA English
- AB The name of the second author, Yaser Rayyan, was misspelled.
- IT 302543-76-6, NCX 2111

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(nitric oxide-donating nonsteroidal anti-inflammatory drugs inhibition of growth of various cultured human cancer cells and evidence of tissue type-independent effect (Erratum))

- RN 302543-76-6 CAPLUS
- CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, α-methyl-4-(2methylpropyl)benzeneacetate (ester) (9CI) (CA INDEX NAME)

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L4
      ANSWER 8 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
      2003:133017 CAPLUS
AN
DN
      138:163547
TI
      Nitrooxy compounds for treatment of vasculopaties
IN
      Del Soldato, Piero
      Nicox S.A., Fr.
PA
      PCT Int. Appl., 26 pp.
SO
      CODEN: PIXXD2
DT
      Patent
LA
      English
FAN.CNT 1
      PATENT NO.
                                KIND
                                         DATE
                                                         APPLICATION NO.
                                                                                       DATE
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PΙ
      WO 2003013499
                                 Α2
                                         20030220
                                                         WO 2002-EP8374
                                                                                       20020726
      WO 2003013499
                                 Α3
                                         20031231
               AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, SG, SI,
                SK, TN, TR, TT, UA, US, UZ, VN, YU, ZA
           RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI IT 2001-MI1744
                                         20010809
                                 Α
      MARPAT 138:163547
OS
      The invention discloses the use for vasculopathy treatment of nitrooxy
AΒ
      compds. (Markush included), or salts thereof. Compds. of the invention
      include e.g. 2-fluoro-\alpha-methyl-4-diphenylacetic acid
      (4-nitrooxy) butyl ester (NO-flurbiprofen).
      302543-75-5 497818-53-8
IT
      RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)
          (nitrooxy compds. for treatment of vasculopaties)
RN
      302543-75-5 CAPLUS
      D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, (\alpha S)-6-methoxy-
CN
      \alpha-methyl-2-naphthaleneacetate (ester) (9CI) (CA INDEX NAME)
```

Absolute stereochemistry.

RN 497818-53-8 CAPLUS CN L-Cysteine, N-acetyl-, 4-(nitrooxy) butyl ester, (αS) -2-fluoro- α -methyl[1,1'-biphenyl]-4-acetate (ester) (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:932594 CAPLUS

DN 138:378736

Nitric oxide-donating nonsteroidal anti-inflammatory drugs inhibit the growth of various cultured human cancer cells: evidence of a tissue type-independent effect

AU Kashfi, Khosrow; Ryann, Yassir; Qiao, Leon L.; Williams, Jennie L.; Chen, Jie; Del Soldato, Piero; Traganos, Frank; Rigas, Basil

CS American Health Foundation, Valhalla, NY, USA

SO Journal of Pharmacology and Experimental Therapeutics (2002), 303(3), 1273-1282

CODEN: JPETAB; ISSN: 0022-3565

PB American Society for Pharmacology and Experimental Therapeutics

DT Journal

LA English

AΒ

IT

The novel nitric oxide (NO)-donating nonsteroidal anti-inflammatory drugs (NO-NSAIDs), which are safer than their NSAID counterparts, inhibit the growth of colon cancer cells with far greater potency than traditional NSAIDs. We examined whether NO-NSAIDs inhibit the growth of cancer cells arising from other human tissues. Human pancreatic, colon, prostate, lung, and tongue cancer cell lines were treated with NO-aspirin, -sulindac, -ibuprofen, and -indomethacin or their traditional counterparts. We determined IC50 values, cell proliferation, apoptosis, cell cycle, cyclooxygenase (COX) protein levels, and morphol. changes (light and electron microscopy). All NO-NSAIDs inhibited the growth of all cancer cell lines studied. The potency of NO-NSAIDs was 11- to 6000-fold greater than that of their counterparts (except for the effect of sulindac on lung cancer cells). NO-aspirin was consistently the most potent NO-NSAID in all cell lines tested (except for the lung cancer cell line), sometimes in excess of 100-fold over the other three NO-NSAIDs. NO-NSAIDs inhibited cell proliferation, induced apoptosis, and altered cell cycle phase distribution (G2/M to G0/G1 block). All altered cellular morphol., whereas NO-aspirin induced nuclear disintegration ("atypical" cells) established by electron microscopy. NO-aspirin showed similar effects on two pancreatic cancer cell lines, BxPC-3 (expresses COX) and MIA PaCa-2 (no COX expression), suggesting a COX-independent effect. NO-NSAIDs showed a tissue-type-independent effect. Their pleiotropic effects involve cell renewal, cell death, and cell cycle phase transitions. results raise the possibility that NO-NSAIDs possess chemopreventive and/or chemotherapeutic activity against a wide variety of human cancers. 302543-76-6, NCX 2111

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(nitric oxide-donating nonsteroidal anti-inflammatory drugs inhibition of growth of various cultured human cancer cells and evidence of tissue type-independent effect)

RN 302543-76-6 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, α -methyl-4-(2-methylpropyl)benzeneacetate (ester) (9CI) (CA INDEX NAME)

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
ANSWER 10 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
L4
      2002:888544 CAPLUS
AN
      137:369833
DN
ΤI
      Preparation of nitrooxy cysteine derivatives for the Alzheimer's disease
      Del Soldato, Piero
IN
      Nicox S.A., Fr.
PA
      PCT Int. Appl., 58 pp.
SO
      CODEN: PIXXD2
DT
      Patent
      English
LA
FAN.CNT 1
      PATENT NO.
                                KIND
                                          DATE
                                                         APPLICATION NO.
                                                                                       DATE
                                _ _ _ _
                                                         -----
      WO 2002092072
PΤ
                                 A2
                                          20021121
                                                         WO 2002-EP5165
                                                                                       20020510
      WO 2002092072
                                 Α3
                                          20030501

    W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA,

                 US, UZ, VN, YU, ZA
           RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
                 GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
                 GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI IT 2001-MI985
                                 Α
                                         20010515
OS
      MARPAT 137:369833
GΙ
```

Me HN
$$O-(CH_2)_4-ONO_2$$
MeO O II

Title compds. A-Bn-Cm-NO2 [n, m = 0-1 with the proviso that m, n cannot be contemporaneously equal to 0; A = R-T1; R = (hetero)cycle; T1 = (CO)0-1, X0-1; X = 0, S, amino; B = T2-X2-T3; T2-3 = CO, X, etc.; X2 = bivalent linking group; C = bivalent linking radical; I] were prepared For instance, 6-methoxy- α -methyl-2-naphthalenacetic acid was coupled to (S)-N-acetylcysteine (DMF/CHCl3, CDI, 12 h), the product converted to the 4-bromobutyl ester (THF, Ph3P, CBr4, 24 h) and that intermediate treated with AgNO3 (CH3CN, reflux, 7 h) to afford II. Nitrooxy derivs. of the invention are effective in inhibiting LPS-induced neurodegeneration and are useful in the treatment of Alzheimer's disease.

IT 302543-75-5P 302543-76-6P 302543-77-7P 475561-35-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nitrooxy cysteine derivs. and related analogs for Alzheimer's disease)

RN 302543-75-5 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, (α S)-6-methoxy- α -methyl-2-naphthaleneacetate (ester) (9CI) (CA INDEX NAME)

RN 302543-76-6 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy) butyl ester, α -methyl-4-(2-methylpropyl) benzeneacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 302543-77-7 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, 2-fluoro- α -methyl[1,1'-biphenyl]-4-acetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 475561-35-4 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, 2-[(2,6-dichlorophenyl)amino]benzeneacetate (ester) (9CI) (CA INDEX NAME)

```
2002:293592 CAPLUS
ÀΝ
     136:325420
DN
TI
     Drugs for diabetes, especially type 2, comprising an antiinflammatory or
     analgesic drug, selected bivalent linkers, and a nitrate ester
     Del Soldato, Piero
IN
     Nicox S.A., Fr.
PA
     PCT Int. Appl., 66 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                          KIND
                                 DATE
                                              APPLICATION NO.
                                                                      DATE
                          - - - -
PΤ
     WO 2002030867
                           A2
                                 20020418
                                             WO 2001-EP11665
                                                                      20011009
     WO 2002030867
                           Α3
                                 20020725
         W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ,
             EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT,
             LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA,
             US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     IT 1319201
                           B1
                                 20030926
                                             IT 2000-MI2201
                                                                      20001012
     CA 2425655
                           AA
                                 20020418
                                             CA 2001-2425655
                                                                      20011009
     AU 2002014006
                           A5
                                 20020422
                                             AU 2002-14006
                                                                      20011009
     EP 1324974
                           A2
                                 20030709
                                             EP 2001-982414
                                                                      20011009
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004511456
                           T2
                                 20040415
                                              JP 2002-534256
                                                                      20011009
     US 2004023890
                           Α1
                                 20040205
                                             US 2003-398511
                                                                      20030411
PRAI IT 2000-MI2201
                           А
                                 20001012
     WO 2001-EP11665
                           W
                                 20011009
OS
     MARPAT 136:325420
GΙ
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-- ANSWER 11 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

Useful for the treatment of diabetes, particularly type 2, are compds. or salts thereof, having the following general formula A-(B)n-(C)m-NO2 [I; wherein A = radical of a drug having an antiinflammatory or analgesic activity; B = bivalent linking group wherein the precursor must meet certain tests described in the application; C = another defined bivalent linking group; n and m = 0 or 1, provided that (n + m) = 1 or 2]. I can be used in conjunction with other antidiabetic drugs, particularly insulin. I increase the direct antidiabetic effect of insulin, and reduce complications of diabetes, particularly vascular diseases, retinopathies,

gave

neuropathies, etc.. The values of n and m, i.e., the presence or absence of bivalent linkers B and C, alone or in combination, are based on performance of the precursors of the linkers in certain tests (no data). These tests are designated as follows: (test 4A): inhibition by > 15% of hemolysis of rat erythrocytes induced by cumene hydroperoxide; (test 5): inhibition of radical production by ≥ 50% in the oxidative degradation of desoxyribose in aqueous Fe2+(NH4)2(SO4)2/thiobarbituric acid solution; and (test

4): inhibition by \geq 50% of DPPH-induced radical production in MeOH solution For instance, acetylsalicylic acid chloride was esterified with 3-(hydroxymethyl)phenol (80%), followed by nitation of the resultant Ph ester with HNO3/H2SO4 (82%), to give invention compound II, which is thus the 3-(nitrooxymethyl)phenyl ester of aspirin. When tested on isolated aorta from insulin-resistant rats, compound II at a concentration of 10-4 M

70% vasorelaxation, relative to non-insulin-resistant controls. This effect was unchanged by the presence or absence of the irreversible NO synthetase inhibitor LNNA. In contrast, both Na nitroprussiate and the indomethacin analog of II, known NO donors, were inactive, and the antidiabetic drug metformin was inactivated by LNNA. 302543-76-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of antidiabetic agents comprising antiinflammatory or analgesic drugs, selected bivalent linkers, and nitrate esters)

RN 302543-76-6 CAPLUS

D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, α -methyl-4-(2-methylpropyl)benzeneacetate (ester) (9CI) (CA INDEX NAME)

```
ANSWER 12 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
L4
ΑN
     2002:293591 CAPLUS
DN
     136:309852
TI
     Preparation of nitrooxyalkylarenes as antiinflammatories and anticancer
     Del Soldato, Piero; Benedini, Francesca; Antoquazza, Patrizia
IN
PΑ
     Nicox S.A., Fr.
SO
     PCT Int. Appl., 72 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                            KIND
                                     DATE
                                                  APPLICATION NO.
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PΙ
     WO 2002030866
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
               BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     IT 1319202
                              В1
                                     20030926
                                                  IT 2000-MI2202
                                                                              20001012
     CA 2425649
                              AΑ
                                     20020418
                                                   CA 2001-2425649
                                                                              20011009
     AU 2002015932
                              A5
                                     20020422
                                                   AU 2002-15932
                                                                              20011009
     EP 1339665
                              Α1
                                     20030903
                                                   EP 2001-986670
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          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
               IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004511455
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                                                   JP 2002-534255
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                                                   US 2003-398289
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PRAI IT 2000-MI2202
                             Α
                                     20001012
     WO 2001-EP11664
                              W
                                     20011009
OS
     MARPAT 136:309852
AB
     AX1LWpNO2 [p = 0, 1; A = RT1; R = specified precursor drug radicals; T1 =
      (CO)t, Xtt; X = O, S, imino, etc.; X1 = TbYTbb; Tb = CO, X; Tbb = (CO)xx,
     Xxxx; t, tt, xx, xxx = 0, 1; Y, Yt = specified bivalent linker; W = YtO;
     with provisos], were prepared Thus, acetylsalicylic acid in DMF was treated
     with NaOEt; after 30 min. the solution was added to a solution of
     bis(chloromethyl)pyridine (preparation given) in DMF; the mixture was kept 7
days
     to give 2-acetyloxybenzoic acid 6-chloromethyl-2-methylpyridinyl ester.
     The latter was heated with AgNO3 in MeCN at 80° for 30 min. to give
     2-acetyloxybenzoic acid 6-nitrooxymethyl-2-methylpyridinyl ester. The
     latter at 10 µM gave 100% inhibition of HT29 cancer cells.
IT
     302543-75-5
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)
         (preparation of nitrooxyalkylarenes as antiinflammatories and anticancer
         drugs)
RN
     302543-75-5 CAPLUS
CN
     D-Cysteine, N-acetyl-, 4-(nitrooxy) butyl ester, (aS)-6-methoxy-
     \alpha-methyl-2-naphthaleneacetate (ester) (9CI) (CA INDEX NAME)
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RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
ANSWER 13 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
L4
     2000:742053 CAPLUS
ΑN
DN
     133:310142
TT
     Synthesis, activity and formulations of pharmaceutical compounds for
     treatment of oxidative stress and/or endothelial dysfunction
     Del Soldato, Piero
IN
PΑ
     Nicox S.A., Fr.
     PCT Int. Appl., 159 pp.
SO
     CODEN: PIXXD2
DT
     Patent
     English
LΑ
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                             APPLICATION NO.
                                                                    DATE
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PΙ
     WO 2000061537
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             NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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                                             EP 2000-925203
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             IE, SI, LT, LV, FI, RO
     JP 2002541233
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                                             NZ 2000-514267
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     ZA 2001008127
                          Α
                                20030103
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                                                                    20011003
     NO 2001004927
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                                20011213
                                                                    20011010
PRAI IT 1999-MI753
                          Α
                                19990413
                                20000411
     WO 2000-EP3234
                          W
os
     MARPAT 133:310142
     Compds. A-B-C-N(0)s and A-C1[N(0)s]-B1 or their salts [s is an integer 1 \,
AB
     or 2, preferably s = 2; A is the radical of a drug and is such as to meet
     the pharmacol. tests reported in the description; C and C1 are two
     bivalent radicals; the precursors of the radicals B and B1 are such as to
     meet the pharmacol. test reported in the description] were prepared for use
     as pharmaceuticals. Thus, (S,S)-N-acetyl-S-(6-methoxy-\alpha-methyl-2-
     naphthalenylacetyl)cysteine 4-nitroxybutyl ester was prepared (NCX 2101)
     from naproxene and N-acetylcysteine in the first of 28 synthetic examples
     given. Pharmacol. test examples and tabular data are also given.
TT
     302543-75-5P, NCX 2101 302543-76-6P, NCX 2111
     302543-77-7P, NCX 2131 302543-81-3P, NCX 2136
     302543-98-2P, NCX 2061
     RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
     effector, except adverse); BSU (Biological study, unclassified); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
     PREP (Preparation); USES (Uses)
        (synthesis, activity and formulations of pharmaceutical compds. for
        treatment of oxidative stress and/or endothelial dysfunction)
RN
     302543-75-5 CAPLUS
     D-Cysteine, N-acetyl-, 4-(nitrooxy) butyl ester, (\alpha S)-6-methoxy-
CN
     \alpha-methyl-2-naphthaleneacetate (ester) (9CI) (CA INDEX NAME)
```

RN 302543-76-6 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, α-methyl-4-(2-methylpropyl)benzeneacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 302543-77-7 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, 2-fluoro- α -methyl[1,1'-biphenyl]-4-acetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 302543-81-3 CAPLUS

CN D-Cysteine, N-acetyl-, 4-(nitrooxy)butyl ester, $(\alpha S)-\alpha$ -(2-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridine-5(4H)-acetate (ester) (9CI) (CA INDEX NAME)

RN 302543-98-2 CAPLUS

CN D-Valine, 3-[[[2-[(2,6-dichlorophenyl)amino]phenyl]acetyl]thio]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)

```
L4 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
```

AN 1996:681459 CAPLUS

DN 125:328304

TI Preparation of nitric esters of 2-(2,6-dihalophenylamino)phenylacetoxyacet ic acid derivatives

IN Serra, Masia Xavier; Pi Sallent, Joan

PA Prodes, S.A., Spain

SO Eur. Pat. Appl., 16 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

ran.	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI		A1	19961023	EP 1996-106009	19960417
	EP 738706	B1	19981007		
	R: AT, BE, CH,	DE, DK	, ES, FI, FR	, GB, GR, IE, IT, LI,	LU, MC, NL,
	PT, SE		•		, , ,
	ES 2092962.	A1	19961201	ES 1995-756	19950419
	ES 2092962	B1	19970716		
	AU 9650428	A1	19961031	AU 1996-50428	19960401
	AU 683790	B2	19971120		
	ZA 9602981	A	19961022	ZA 1996-2981	19960415
	CA 2174287	AA	19961020	CA 1996-2174287	19960416
	CN 1138027	A	19961218	CN 1996-105067	19960417
	AT 171936	E	19981015	AT 1996-106009	19960417
	NO 9601537	A	19961021	NO 1996-1537	19960418
	JP 09020738	A2	19970121	JP 1996-98815	19960419
	US 5844696	A	19981201	US 1996-634763	19960419
	BR 9603235	A	19980428	BR 1996-3235	19960731
PRAI	ES 1995-756	Α	19950419		
OS GI	CASREACT 125:328304;	MARPA'	Г 125:328304		

AB The title compds. [I; A = F, Cl, Br; X = O, NH, NR (R = Cl-8 alkyl); R1, R2 = Cl-8 alkyl, n = 1-10], potentially useful as antiinflammatory agents (no data), were prepared by condensation of 2-(2,6-dihalophenylamino)phenylacetoxyacetic acid with a compound Y-(C)nR1R2ONO2 [Y = OH, NH2, NHR] in the presence of condensing agent such as N,N'-carbonyl

Ι

diimidazole in an aprotic organic solvent.
IT 183195-07-5P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

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(preparation of nitric esters of 2-(2,6-dihalophenylamino)phenylacetoxyacetic acid derivs.)

RN 183195-07-5 CAPLUS

CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[4-(nitrooxy)butoxy]-2-oxoethyl ester (9CI) (CA INDEX NAME)

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